REMARKS

The Examiner has rejected claims 50-54 and 69 under 35 U.S.C. 102(e) as being anticipated by Burshteyn et al. (US Pub. No. 2002/0123154).

For context, a disclosed embodiment of Applicant's device will first be discussed without limitation of the claims. Applicant's Fig. 5 depicts a schematic of steps that can be included in preparing a macromolecule sample. The liquid mixture 202 contains a macromolecule 104, and can also contain fine components 213, e.g., salts, molecules smaller than the macromolecule, and the like; and rough components 207, e.g., cells, cell fragments, particulate contaminants, molecules larger than the macromolecule, and the like. Macromolecule 104 can be dissolved in the liquid mixture, or can be partially contained in cells, as depicted. Optional lysis step 204 lyses at least a portion of the cells to release macromolecule 104.

A rough separation step 410 applies the liquid mixture to a rough filter membrane 412, and a pressure differential across the filter membrane 412 directs at least a portion of the liquid, macromolecule 104, and the fine components 213 through the filter membrane, separating at least a portion of rough components 207 at rough filter 412. Rough filter membrane 412 can be selected to remove at least a portion of components that are larger than the macromolecule, e.g., greater in diameter or molecular weight.

A fine separation step 414 applies the liquid mixture to a fine filter membrane 416, and a pressure differential across the filter membrane directs at least a portion of the liquid and the fine components 213 through the filter membrane to waste 418, separating at least a portion of macromolecule 104 at the filter membrane. Fine filter membrane 416 can be selected to remove at least a portion of components that are smaller than the macromolecule, e.g., salt components.

Advantageously, the filters and filtration methods employ the technique of "back-flushing." That is, each filter membrane can be cleaned by directing a fluid, e.g., a buffer, a cleaning fluid, water, a solvent, a desalination buffer, a denaturation buffer, combinations thereof, and the like across the filter membranes in a direction opposite to a previous filtration step. For example, once the macromolecule has gone through the rough filtration step, a liquid can be directed across the rough filter membrane in a direction opposite to the direction of

filtration. This cleans the filter membrane surface to restore it to its initial capacity and characteristics.

Also, in order to direct the macromolecule to the denaturization vessel, once the macromolecule has gone through the fine filtration step, valve 522 opens and pump 518 draws a portion of buffer from reservoir 524. Valve 522 closes, valve 510 opens, and pump 518 directs the buffer across the filter membrane 416 in a direction opposite to the direction of filtration. Preferably, pumps 518 and 506 operate cooperatively to direct the buffer across the filter membrane 416, and pump 506 then directs the mixture through valve 520. Addition of the buffer across the filter membrane can dislodge portions of macromolecule 104 that may become associated with fine filter membrane 416 in the fine filtration step.

Burshteyn describes an apparatus and method for removing interferents from a test sample containing a mixture of a composition of interest and interferents in an automated apparatus. As shown in Burshteyn's Figures 2 and 3, the filtration device 24 includes a microporous hollow fiber membrane 60 having a plurality of pores 65 sized to retain the composition of interest while allowing smaller diameter interferents to pass through the membrane. As shown in Fig. 3, a sample of cells is shown in lumen 66 as a mixture comprising cells 74 and interferents 72. The mean diameter of the pores 65 is smaller than the diameter of the cells of interest, but greater than the diameter of interferents, thus allowing the interferent, to pass through the pores while the cells of interest, or larger diameter cells 74 remain in the lumen 66.

As shown in Figure 4G, a buffer 49 is then dispensed from the buffer reservoir 46 through the filtration device into the sample container 16. Movement of buffer through the device flushes the desired sample of cells from the lumen 66 into the sample container 16. Detergent can also be similarly run through the filtration device through the lumen 66 and to clean it after each sample, after a predetermined number of samples, or upon fouling of the membrane 60.

The Examiner states that Burshteyn describes directing a liquid through a filter in a direction opposite to the direction of filtration. Applicant respectfully disagrees.

The Examiner cites to Burshteyn's paragraph 85 for support. Paragraph 85 states that recovery of the cells from the filter can be accomplished by providing a force, such as a flow of

liquid, to the filter in a direction opposite the direction from which the blood cell sample contacted the filter in step 80. In step 80, a vacuum force is applied to pull the sample into the lumen 66 of the filter. It then comes in contact with the tangential filter membranes 60. The sample contacts the filter by being pulled from the sample container up into the lumen 66. Thus, if a force is applied opposite to the direction from which the sample contacts the filter, the force should move downwards through the lumen of the filters to push it back into the sample container.

In every embodiment, therefore Burshteyn's buffer is directed downward through the lumen to simply push the sample into the sample container. It is not directed across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis. If it was, the buffer would be aimed directly through Burshteyn's side membranes 60, and not from the top of lumen to simply flush the sample downward into the sample container.

Further, the flow of Burshteyn's buffer is substantially parallel to the faces of the membranes. In contrast, the flow of Applicant's liquid is across the filter membrane.

Thus, Burshteyn does not describe all the limitations of amended independent claims 50 and 69. Specifically , Burshteyn does not describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis . Thus, these claims or any claims dependent on these claims are allowable for at least these reasons.

103(a) Rejections

Dependent claims 22-31, 32-35, 41-43, and 68 have been rejected under 103(a) by the Examiner as being unpatentable over Burshteyn in view of Sparks, U.S. 6,637,257.

As shown in Sparks' figures 1 and 2, a substrate 12 has micromachined vias 14 that extend through the thickness of the substrate 12. As shown in figures 3 and 4, multiple substrates can be utilized in a single filtering device 10 or 110. The upper most substrate 12 has vias sized to filter relatively large cells or particles, while the middle and lower substrates 12 are sized to filter smaller particles. A manual or automatic back-flushing operation can be

performed to remove the cells/particles that have collected at the upstream surface 16 as the need requires (Sparks, col. 6, lines 11-13).

Firstly, one would not look to combine Burshteyn's device with Spark's device. Burshteyn's device is a tangential type filter that is targeted towards filtration of blood cells, where only the larger particles are of interest for analysis. Burshteyn nowhere describes the need to analyze smaller particles. Spark's device is intended to be a multi-phase filtration system for separating larger and smaller particles in steps. Thus, one would not look to combine Burshteyn's one-phase tangential filter with Spark's multi-phase filter.

Further, even if one were to combine these devices, they do not describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, as is described by the Applicant. As previously stated, Burshteyn does not describe this limitation. Sparks also does not describe this limitation.

Thus, neither Sparks nor Burshteyn describe all of the limitations of amended claim 22. Specifically, neither describe directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration, the macromolecule this being directed further in the apparatus for analysis . Therefore, claim 22 or any claim dependent on the same is allowable for at least that reason.

Dependent claim 36 has been rejected as being unpatentable over Burshteyn in view of Holmes (US 4830969). Holmes does not describe any of the limitations of claim 22 that are absent in Burshteyn's or Spark's device. Thus, dependent claim 36 is allowable over Burshteyn, Sparks, and Holmes either alone or in combination.

Dependent claims 37-40 have also been rejected over Burshteyn in view of Sparks and in further view of Shnipelsky et al (Schnipelsky, US 6645758).

As stated, neither Burshteyn nor Sparks alone or in combination describe all of the limitations of independent claim 22. Similarly, Shnipelsky does not describe any of the limitations of claim 22 that are absent in Spark's or Burshteyn's devices. Dependent claims 37-40 are allowable for at least these reasons.

Also, dependent claim 55 has also been rejected as being unpatentable over Burshteyn in view of Schnipelsky. Shnipelsky either alone or in combination with Burshteyn also does not describe all of the limitations of independent claim 50, on which claim 55 is dependent.

Specifically, neither reference describes the step of directing a liquid across the fine filter membrane in a direction opposite to the direction of filtration. Thus, dependent claim 55 is allowable for at least this reason.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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